IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant   :   Jonathan M Friedman

Identification Information   :   Non-Provisional Application based on Provisional
Application – 60/219,863 filed on July 20, 2000

Filed   :   Herewith

For   :   **A METHOD FOR *AB INITIO* DETERMINATION OF MACROMOLECULAR CRYSTALLOGRAPHIC PHASES AT MODERATE RESOLUTION BY A SYMMETRY-ENFORCED ORTHOGONAL MULTICENTER SPHERICAL HARMONIC-SPHERICAL BESSEL EXPANSION**

Docket No.
389004/0039
JJD:BVO:cp

July 20, 2001

PRELIMINARY AMENDMENT

Assistant Commission for Patents
Washington D.C. 20231

Sir:

Prior to examination of the above-referenced Application, please amend the Application as follows:

IN THE DRAWINGS

On page 2, last line after the words "tetragonal Staphylococcal nuclease" please insert the following:

SSL-DOCS1 1130726v1

-- BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows a first protein crystal packing function histogram utilizing the method of the invention and based on providing the number of possible configurations for a given protein or other molecule of interest with a resolution in Angstroms.

FIG. 2 shows a second protein crystal packing function histogram utilizing the method of the invention and based on providing the number of possible configurations for a given protein or other molecule of interest with a resolution in Angstroms.

FIG. 3 shows a flow chart for the calculation routine of the current invention used to resolve the unphased diffraction amplitudes of the SHSB representations of the current invention.

FIG. 4 shows a space filling schematic for a mathematical representation of the orthorhombic space group of the invention.

FIG. 5 shows a flow chart for the calculation routine of the current invention used to resolve the unphased diffraction amplitudes of the SHSB representations into a Fourier Transformation of the model crystal of the molecule of interest utilizing a fractionalization matrix.

FIG. 6 shows a representation of an Expanded Direct Space Basis Function of the invention.

FIG. 7 shows a representation of a Component Direct Space Basis Function of the invention and the Component Fourier Transformations following there from. --

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IN THE SPECIFICATION:

On Page 4, last full paragraph, after the words "lower than 55%" please delete the phrase "(Matthews, 1968xxx)" and insert in its place -- (Matthews, B.W., J.Mol.Biol. 33, 491-497 (1968) --

On Page 4, in the footnote on the bottom of the page, after the words "in quantum mechanics" please delete the phrase "(Cohen-Tannoudji, et al. 1980)" and insert in its place -- Cohen-Tannoudji, C., Diu, B., Laloë, pp. 21-28 in Quantum Mechanics, Vol. I, John Wiley and Sons: New York (1977) --

On Page 5, line 1 please delete the phrase "(Wang, 197xxx)" and insert in its place -- Wang, B.C., Meth.Enzymology 115, 90-112 (1985) --

On Page 9, first full paragraph, after the words "Protein Database" please delete the phrase "(ref xxx)" and insert in its place – (Abola, E.E., Bernstein, F.C. and Koetzie, T.F. (1988) in Computational Molecular Biology, Sources and Methods for Sequence Analysis (Lesk, A.M. ed.), pp. 69-81; and, H.M. Berman, J. Westbrook, Z. Feng, G. Gilliland, T.N.Bhat, H. Weissig, I.N. Shindyalov, P.E. Bourne: The Protein Data Bank. Nucleic Acids Research, 28 pp.235-242 (2000)) --

On Page 9, first full paragraph, after the words "deficiencies in this procedure. Shown in" please delete the phrase "Fig. XXX" and insert in its place -- Fig. 1 --

On Page 9, first full paragraph, after the words "coordinate of each of those" please delete the letters "xxxx"

On Page 10, first full paragraph, after the words "near the top 20" please delete the letters "(30%xxx)" and insert in its place – (30%) --

On page 10, first full paragraph, after the words "the histogram of distances in" please delete the phrase "Fig. xx" and insert in its place -- Fig. 2 --

On Page 11, third full paragraph, after the words "basis functions are known" please delete the phrase "(Friedman, 1998; Crowther, 19xx; Dodson, 19xx)" and insert in its place -- (Friedman 1999; Crowther, R.A., 1972; Rossman, M.G., 1972; Dodson, E., 1985) --

On Page 11, third full paragraph, after the words "a robust recursion formula" please delete the phrase "(ref)" and insert in its place -- (Press, W.H, et al., (1988)) --

On Page 13, line 3, after the words in the parenthetical "assumptions compare Podjarny" please delete the phrase "et al., 199x" and insert in its place -- Podjarny, A.D., Urzhumtsev, A.G., Navaza, J. Trans.Amer.Cryst.Assoc. 30, 109-120 (1994); Dorset, D.L., McCourt, M.P., Z.Krystallographie 214, 652-658 (1999).

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On Page 17, last line of numbered paragraph (1) after the words "are shown in" please delete the words "Fig. XXX" and insert in its place – Table II --

On Page 18, third line after the words "by the calculation]." please delete the words "Fig. XXX."

On Page 18, numbered paragraph (2) after the words "lower m index (See eg." please delete the words "table. XX" and insert in its place – Table I --

On Page 19, first full paragraph, after the words "style electron density maps" please delete the phrase "(R.Reed xxxx)" and insert in its place -- (Read, R.J. Acta Cryst. A42, 140-149 (1986); Read, R.J. Acta Cryst. A46, 140-149 (1990); Read, R.J. Acta Cryst. A46, 900-912 (1990))

On Page 19, first full paragraph, after the words "map using Sim weights" please delete the phrase "(ref to Sim xxx)" and insert in its place -- (Sim, G.A. Acta Cryst. 12, 813-815 (1959); Sim, G.A. Acta Cryst. 13, 511-512 (1960)).

On Page 20, lines 3 and 4, after the words "phasing the P41 form of" please delete the phrase "Staphalococcal Nuclease at 2.8 Å (xxxx unique" and insert in its place the words – Staphylococcal Nuclease 2.8 Å (15118 unique --

On Page 20 lines 6 and 7, numbered paragraph (1) after the words "under determination" please delete the words "(xxxx data, xxx SHSB amplitudes, xxxxx SHSB signs, xxxx SHSB phases)" and insert in its place the words -- (15118 data (2.70 Å), model (2.70 Å with a contrived m cutoff), 3539 SHSB amplitudes, 427 SHSB signs, 3112 SHSB phases) --

On Page 20 lines 8 and 9, numbered paragraph (2) after the words "diffraction data" please delete the words "(xxxx data, xxx SHSB amplitudes, xxxxx SHSB signs, xxxx SHSB phases)" and insert in its place the words -- (15118 data (2.70 Å), model (2.70 Å with 14136 total parameters), 7068 SHSB amplitudes, 427 SHSB signs, 6636 SHSB phases) --

On Page 20 line 13, numbered paragraph (3) after the words "Å diffraction data" please insert the words -- The full Crowther equation data 2.70 Å diffraction data (15118 data (2.70Å); model (3.40Å): 7094 total parameters consisting of 3547 SHSB amplitudes, 269 SHSB signs, 3278 SHSB phases. --
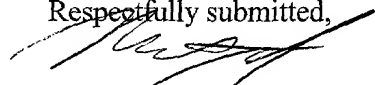
REMARKS

Applicants respectfully request that the amendments above be entered prior to substantive examination of the utility application filed herewith. These amendments are made

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to clarify the specification as provided in the utility application filed herewith and are supported by the specification as filed provisionally on July 20, 2000. The utility application filed herewith represents the conversion of the current case from provisional filing status to utility status and entrance into substantive prosecution. It is Applicant's belief that the specification as originally filed provisionally fully supports both the claims as provided in the utility application as well as the figure legends added herein.

Applicants respectfully request entry of the above amendments prior to examination of the utility Application. If the Examiner cannot issue an immediate Notice of Allowance, the Examiner is invited to telephone the undersigned attorney with a view towards discussing the outstanding issues. No fee, other than those needed to file this utility application and its claims, is deemed necessary. However, if any additional fee is required, the Assistant Commissioner is hereby authorized to charge the amount of such fee to the undersigned attorney's Deposit Account No. 19-4709.

Early and favorable action is earnestly solicited.

Respectfully submitted,

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